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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
NGUYEN, QUANG	
ART UNIT	**PAPER NUMBER**
1636	

DATE MAILED: 09/07/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/905,114	ZHANG ET AL.	
	Examiner	Art Unit	
	Quang Nguyen, Ph.D.	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 June 2003 and 18 March 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-7,9,11-15 and 57-80* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *1-6,9,11,12,15,57 and 58* is/are allowed.

6)☒ Claim(s) *7 and 59-80* is/are rejected.

7)☒ Claim(s) *13 and 14* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicants' amendments filed on 6/18/03 and 3/18/03 have been entered.

Claims 1-6, 7, 9, 11-15 and new claims 57-80 are pending in the present application, and they are examined on the merits herein.

Claim Objections

It appears that the original claim 13 is inadvertently mislabeled as the second claim 12 in the amendment filed on 3/18/03 (page 4 of the amendment). Appropriate correction is required.

Claim 14 is objected to because of the lack of an article - - a - - in front of the term "yeast cell". Appropriate correction is required.

Written Description

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Amended claim 7 and new claims 59-80 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. **This is a modified rejection necessitated by Applicants' amendment.**

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111 (Fed. Cir. 1991), clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" Vas-Cath Inc. v. Mahurkar, 19USPQ2d at 1117. The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." Vas-Cath Inc. v. Mahurkar, 19USPQ2d at 1116.

Applicant's invention is drawn to an isolated polynucleotide, which hybridizes under recited stringent conditions to the complement of SEQ ID NO:1 or SEQ ID NO:3 and which encodes a fertility associated antigen (FAA), a vector and a host cell comprising the same and a method of producing a fertility associated antigen comprising introducing the same isolated polynucleotide into a cultured host cell under conditions suitable for expression of fertility associated antigen.

The scope of the instant claims encompasses any isolated polynucleotide encoding a fertility associated antigen, as long as it hybridizes to the complement of SEQ ID NO:1 or SEQ ID NO:3 under recited stringent conditions, a vector, a host cell comprising the same and a method of producing a fertility associated antigen using the same isolated polynucleotide. Apart from disclosing the partial bovine cDNA sequence comprising SEQ ID NO:1 or SEQ ID NO:3, the instant specification fails to teach which essential core structure(s) or element(s) possessed by SEQ ID NO:1 or SEQ ID NO:3 that are responsible for any one of the bioactivities associated with a fertility associated antigen (e.g., cryo-protective property and/or enhancing fertility of a sperm), let alone for

any isolated polynucleotide which hybridizes to the complement of SEQ ID NO:1 or SEQ ID NO:3 under the recited hybridizing conditions. It should be noted that any polynucleotide molecule containing a sequence as short as 25-50 identical nucleotides of SEQ ID NO:1 or SEQ ID NO:3 would be able to hybridize to the complement of SEQ ID NO:1 or SEQ ID NO:3 under the recited conditions in light of the teachings of Kennell (Progr. Nucl. Acid Res. Mol. Biol. 11:259-301, 1971) who states that "it would appear that, depending on G + C content, the minimum size for a stable complex is from 10 to 20 nucleotides. The thermal stability rises sharply for longer lengths so that, depending on the G + C content, the stability of a complementary duplex of 25-50 nucleotides approaches that of any much longer complex" (page 261, first paragraph). Moreover, although the cDNA encoding for a macrophage specific DNase I-like endonuclease (Baron et al., Gene 215:291-301, 1998) which is 80.5% identical to SEQ ID NO:1 and 78.5% identical to SEQ ID NO:3, it has never been demonstrated to possess any fertility-associated antigen bioactivity, whereas the cDNAs encoding for the bovine seminal plasma BSP-A3 and BSP-30-kDa (Salois et al., Biology of Reproduction 61:288-297, 1999), known to potentiate the capacitation of spermatozoa, have no significant homology to either SEQ ID NO:1 or SEQ ID NO:3. Thus, there is an apparent lack of a relationship between the structural homology to SEQ ID NO:1 or SEQ ID NO:3 of the present invention with any of the bioactivities associated with a fertility associated antigen. Furthermore, the instant specification also fails to teach a representative number of species for a broad genus of an isolated polynucleotide encoding a fertility associated antigen as claimed.

The claimed invention as a whole is not adequately described if the claims require essential or critical elements which are not adequately described in the specification and which are not conventional in the art as of Applicants' filing date. Possession may be shown by actual reduction to practice, clear depiction of the invention in a detailed drawing, or by describing the invention with sufficient relevant identifying characteristics such that a person skilled in the art would recognize that the inventor had possession of the claimed invention. Pfaff v. Wells Electronics, Inc., 48 USPQ2d 1641, 1646 (1998). The skilled artisan cannot envision the detailed structures of any isolated polynucleotide encoding a fertility associated antigen as broadly claimed, other than a polynucleotide sequence comprising SEQ ID NO:1 or SEQ ID NO:3, a vector, a host cell comprising the same and a method for producing a FAA using the same polynucleotide sequence. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. See *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016 (Fed. Cir. 1991). One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481, 1483.

Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Amended claim 7 and new claims 59-80 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated polynucleotide sequence comprising SEQ ID NO:1 or SEQ ID NO:3 which encodes a

fertility associated antigen, a vector, a host cell comprising the same, and a method of producing a fertility associated antigen in a cultured host cell using the same; does not reasonably provide enablement for any other isolated polynucleotide, vector, host cell and a method of producing a fertility associated antigen as claimed. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims. **This is a modified rejection necessitated by Applicants' amendment.**

The factors to be considered in the determination of an enabling disclosure have been summarized as the quantity of experimentation necessary, the amount of direction or guidance presented, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability of the art and the breadth of the claims. *Ex parte Forman*, (230 USPQ 546 (Bd Pat. Appl & Unt, 1986); *In re Wands*, 858 F.2d 731, 8 USPQ 2d 1400 (Fed. Cir. 1988)).

The instant claims are drawn to an isolated polynucleotide, which hybridizes under recited stringent conditions to the complement of SEQ ID NO:1 or SEQ ID NO:3 and which encodes a fertility associated antigen (FAA), a vector and a host cell comprising the same and a method of producing a fertility associated antigen comprising introducing the same isolated polynucleotide into a cultured host cell under conditions suitable for expression of fertility associated antigen

The specification discloses by exemplification the cloning a partial cDNA sequence (SEQ ID NO:1) encoding the 22 kDa bovine fertility associated antigen (FAA) having amino acids 73 to 269 of the natural intact bovine FAA. Applicants further

demonstrate that the recombinant 22 kDa FAA reduces cryo-damage to the bull sperm and increases fertility of the sperm when used as a semen additive.

The above evidence has been noted and considered. However, the evidence is not reasonably extrapolated to the instant broadly claimed invention for the following reasons.

1. The breadth of the claims

The instant claims encompasses any isolated polynucleotide encoding a fertility associated antigen, as long as it hybridizes to the complement of SEQ ID NO:1 or SEQ ID NO:3 under recited stringent conditions, a vector, a host cell comprising the same and a method of producing a fertility associated antigen using the same isolated polynucleotide.

2. The state and the unpredictability of the prior art

At the effective filing date of the present application (7/14/2000), there is a high degree of unpredictability between the sequence of a polypeptide and its tertiary structure or its activity as evidenced by the teachings of Rudinger (*In* J.A. Parsons, ed. "Peptide hormones", University Park Press, 1976) and Ngo et al. (*In* K. Merz et al., ed. "The protein folding problem and tertiary structure prediction", Birkhauser, 1994, 491-495). In discussing peptide hormones, Rudinger has stated that "The significance of particular amino acids and sequences for different aspects of biological activity can not be predicted a priori but must be determined from case to case by painstaking experimental study (Page 6, first sentence of Conclusions). Moreover, there is an apparent lack of any co-relationship between any structural feature(s) or domain(s)

associated with any bioactivity associated with a fertility-associated antigen in the prior art at the effective filing date of the present application. For example, although the cDNA encoding for a macrophage specific DNase I-like endonuclease (Baron et al., Gene 215:291-301, 1998) which is 80.5% identical to SEQ ID NO:1 and 78.5% identical to SEQ ID NO:3, it has never been demonstrated to possess any fertility-associated antigen bioactivity, whereas the cDNAs encoding for the bovine seminal plasma BSP-A3 and BSP-30-kDa (Salois et al., Biology of Reproduction 61:288-297, 1999), known to potentiate the capacitation of spermatozoa, have no significant homology to either SEQ ID NO:1 or SEQ ID NO:3 of the present invention.

3. The amount of direction or guidance provided

The instant specification is not enabled for the present broadly claimed invention because in order to make and use any sequence variant with the reasonable assurance that it would have the desirable properties of the invention, the artisan would need at least to know which region(s) of the molecule are responsible for the interactions underlying its biological functions. As is well recognized in the art, any modification (even a "conservative" substitution) to a critical structural region of a protein is likely to significantly alter its functional properties. The present disclosure offers no guidance as to which regions of an encoded FAA molecule would be tolerant of alteration and which would not, which "particular" amino acid changes (substitution, deletion or insertion) at which positions and in which combinations, such that the encoded variant FAA proteins having one or more of the bioactivities of natural FAA could still be retained. There is a high degree of unpredictability associated with the make and use of the claimed

embodiment as evidenced by the state and the unpredictability of the prior art discussed above. As set forth in *In re Fisher*, 166 USPQ 18 (CCPA 1970), compliance with 35 USC 112, first paragraph requires:

> That scope of claims must bear a reasonable correlation to scope of enablement provided by specification to persons of ordinary skill in the are; in cases involving predictable factors, such as mechanical or electrical elements, a single embodiment provides broad enablement in the sense that, once imagined, other embodiments can be made without difficulty and their performance characteristics predicted by resort to known scientific laws; in cases involving unpredictable factors, such as most chemical reactions and physiological activity, scope of enablement varies inversely with degree of unpredictability of factors involved.

4. The amount of experimentation provided

Apart from a disclosure of a bovine cDNA sequence comprising SEQ ID NO:1 or SEQ ID NO:3 that encodes a fertility associated antigen, the present specification fails to provide any example demonstrating that any other isolated polynucleotide which hybridizes to the complement of SEQ ID NO:1 or SEQ ID NO:3 under the recited conditions would also encode a fertility associated antigen.

Accordingly, due to the lack of sufficient guidance provided by the specification, regarding to the issues discussed above, the unpredictability of the relevant art, and the breadth of the instant claims, it would have required undue experimentation for one skilled in the art to make and use the instant broadly claimed invention.

Response to Arguments

Applicant's arguments related in part to the above rejections in the Amendment filed on 3/18/03 (pages 7-8) have been fully considered, but they are respectfully found to be unpersuasive.

Applicants refer Examiner's attention the USPTO "Synopsis of Application of Written Description Guidelines", particularly Example 9. Applicants argue that the claim in the Example is similar to claim 7 in terms of providing for a sequence which hybridizes under stringent conditions to an allowable DNA, is adequately described. Therefore, the instant claims are adequately described and enabled because the sequences are described, the conditions for hybridization are described, and the activity of fertility associated antigen is described.

Firstly, unlike the situation in Example 9 in which hybridizing nucleic acids were expressed, and several were shown to encode proteins that bind to a dopamine receptor and stimulate adenylate cyclase activity, the present specification fails to provide any example demonstrating that any isolated polynucleotide which hybridizes to the complement of SEQ ID NO:1 or SEQ ID NO:3 under the recited conditions would also encode a fertility associated antigen, other than SEQ ID NO:1 and SEQ ID NO:3.

Secondly, there is also an apparent lack of a relationship between the structural homology to SEQ ID NO:1 or SEQ ID NO:3 of the present invention with any of the bioactivities associated with a fertility associated antigen. This is because while the cDNA encoding for a macrophage specific DNase I-like endonuclease (Baron et al., Gene 215:291-301, 1998) which is 80.5% identical to SEQ ID NO:1 and 78.5% identical

to SEQ ID NO:3, its encoded product has never been demonstrated to possess any fertility-associated antigen bioactivity, whereas the cDNAs encoding for the bovine seminal plasma BSP-A3 and BSP-30-kDa (Salois et al., Biology of Reproduction 61:288-297, 1999), known to potentiate the capacitation of spermatozoa, have no significant homology to either SEQ ID NO:1 or SEQ ID NO:3. Nor does the instant specification teach which essential core structure(s) or element(s) possessed by SEQ ID NO:1 or SEQ ID NO:3 that are responsible for any one of the bioactivities associated with a fertility associated antigen (e.g., cryo-protective property and/or enhancing fertility of a sperm). Therefore, the instant claims are not adequately described as asserted by Applicants.

Thirdly, in light of over-all state of the relevant art and other Wands factors already discussed above, including the insufficient guidance provided by the present application it would also have undue experimentation for a skilled artisan to make and use the instant broadly claimed invention.

Conclusion

Claims 1-6, 9, 11-12, 15 and 57-58 are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Quang Nguyen, Ph.D., whose telephone number is (571) 272-0776.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's mentor, David Guzo, Ph.D., may be reached at (571) 272-0767, or SPE, Irem Yucel, Ph.D., at (571) 272-0781.

To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1636; Central Fax No. (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

DAVID GUZO
PRIMARY EXAMINER